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EXAMINER	
NGUYEN, QUANG	
ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 04/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/706,798	CROCE ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-74 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-74 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-74 are pending in the present application, and they are subjected to the following restrictions.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

Group Restriction

I. Claims 1-4, drawn to a method of diagnosing an miR15 mediated cancer in a subject comprising measuring the level of miR15 gene product in a sample, classified in class 435, subclass 6.

II. Claims 1-4, drawn to a method of diagnosing an miR16 mediated cancer in a subject comprising measuring the level of miR16 gene product in a sample, classified in class 435, subclass 6.

III. Claims 5-7, drawn to a method of diagnosing an miR15 mediated cancer in a subject comprising analyzing an miR15 gene product in a sample for deletions or mutations, classified in class 435, subclass 6.

IV. Claims 5-7, drawn to a method of diagnosing an miR16 mediated cancer in a subject comprising analyzing an miR16 gene product in a sample for deletions or mutations, classified in class 435, subclass 6.

V. Claims 8-13, drawn to a method of diagnosing an miR15 mediated cancer in a subject comprising measuring an miR15 gene copy number in a sample, classified in class 435, subclass 6.

VI. Claims 8-13, drawn to a method of diagnosing an miR16 mediated cancer in a subject comprising measuring an miR16 gene copy number in a sample, classified in class 435, subclass 6.

VII. Claims 14-15, 18-25, 30-39, 50-51, 53, 58-60 and 61-70, drawn to a method of treating an miR15 mediated cancer in a subject in need of such treatment comprising administering to the subject an effective amount of an isolated miR15 gene product and a pharmaceutical composition comprising an isolated miR15 gene product, classified in class 514, subclass 44.

VIII. Claims 14-15, 18-25, 30-39, 50-51, 53, 58-60 and 61-70, drawn to a method of treating an miR16 mediated cancer in a subject in need of such treatment comprising administering to the subject an effective amount of an isolated miR16 gene product and a pharmaceutical composition comprising an isolated miR16 gene product, classified in class 514, subclass 44.

IX. Claims 25-29 and 53-57, drawn to a method of treating an miR15 mediated cancer in a subject in need of such treatment comprising administering to the subject an effective amount of a nucleic acid encoding or expressing an isolated miR15 gene product, classified in class 514, subclass 44.

X. Claims 25-29 and 53-57, drawn to a method of treating an miR16 mediated cancer in a subject in need of such treatment comprising

administering to the subject an effective amount of a nucleic acid encoding or expressing an isolated miR16 gene product, classified in class 514, subclass 44.

XI. Claims 16-17, 40-49 and 52, drawn to a method of treating an miR15 mediated cancer in a subject in need of such treatment using autologous cells transfected with a nucleic acid comprising sequence encoding an effective amount of an miR15 gene product, classified in class 424, subclass 93.21.

XII. Claims 16-17, 40-49 and 52, drawn to a method of treating an miR16 mediated cancer in a subject in need of such treatment using autologous cells transfected with a nucleic acid comprising sequence encoding an effective amount of an miR16 gene product, classified in class 424, subclass 93.21.

XIII. Claims 71-74, drawn to a pharmaceutical composition comprising a nucleic acid encoding an isolated miR15 gene product, classified in class 514, subclass 44.

XIV. Claims 71-74, drawn to a pharmaceutical composition comprising a nucleic acid encoding an isolated miR16 gene product, classified in class 514, subclass 44.

The inventions are distinct, each from the other because of the following reasons:

Inventions I-XII are directed to distinct methods having different starting materials, different method steps and different desired end-results or outcomes, and

therefore they would require different technical considerations. For example, the diagnostic methods of Groups I-VI are distinct one from the others depending on whether a method requires the step of measuring the level of miR15 or miR16 gene product, analyzing an miR15 or miR16 gene product for deletions or mutations, and for measuring an miR15 or miR16 gene copy number. It is further noted that the miR15 gene product is distinct from the miR16 gene product as evidenced by their distinct sequences. None of the diagnostic methods of Groups I-VI requires any therapeutic effect as the methods of Groups VII-XII. The treatment methods of Groups VII-VIII are distinct from the treatment methods of Groups IX-X and XI-XII because the methods of Groups VII-VIII require the administration of an isolated miR15 or miR16 gene product into a treated subject, whereas the methods of Groups IX-X requires the administration of a nucleic acid encoding or expressing an isolated miR15 or miR16 gene product and the methods of Groups XI-XII involve the administration of autologous cells transfected with a nucleic acid comprising sequence encoding an effective amount of either miR15 or miR16 gene product. Please note as defined by the instant specification, the term "an miR15 or miR16 gene product" means the processed or unprocessed RNA transcripts from the miR15 or miR16 genes (page 12, lines 13-15). Therefore, a nucleic acid encoding or expressing an isolated miR15 and miR16 gene product (e.g., a recombinant plasmid or a recombinant viral vector) is distinct chemically and physically from the isolated miR15 or miR16 gene product (basically RNA transcripts). Accordingly, claims 16-17, 26-29, 52, 54-57 and an embodiment of claims 25 and 53 are improperly dependent on independent claims 14 and 50. The treatment method of

Group VII is distinct from the treatment method of Group VIII because it involves different starting materials (e.g., isolated miR15 vs isolated miR16; patient with an miR15 mediated cancer vs patient with an miR16 mediated cancer). Similar, the treatment method of Group IX or XI is distinct from the treatment method of Group X or XII, respectively, for the same reasons.

The pharmaceutical products of Groups XIII-XIV are not required in the practice of any of the methods of Groups I-VIII and XI-XII. The pharmaceutical composition of Group XIII is distinct from the pharmaceutical composition of Group XIV because it contains a nucleic acid encoding an isolated miR15 gene product instead of a nucleic acid encoding an isolated miR16 gene product.

Inventions XIII-XIV and IX-X are related as product and process of use; respectively. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case, the pharmaceutical compositions of either Groups XIII or Group XIV can be used to transfect cells (xenogeneic, allogeneic or autologous cells) *ex vivo*, prior to the implantation of the genetically modified cells into a patient in need thereof.

Because these inventions are distinct for the reasons given above, and separate search requirements due to the distinctness of each Invention as discussed above in both **patented and non-patented literature**. Therefore, it would be unduly burdensome for the examiner to **search and/or consider the patentability**

(examination) of all the inventions in a single application. Accordingly, restriction for examination purposes as indicated is proper.

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17 (h).

Species Restriction

I. Should Applicants elect either Group I or Group II, this application contains claims directed to the following patentably distinct species of an assay:

A specifically named assay recited in the Markush group of claim 2.

The species are independent or distinct because they are distinct assays having distinct assay steps and materials.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, at least claims 1-4 are generic.

II. Should Applicants elect either Group III or Group IV, this application contains claims directed to the following patentably distinct species of an assay:

A specifically named assay recited in the Markush group of claim 6.

The species are independent or distinct because they are distinct assays having distinct assay steps and materials.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, at least claims 5-7 are generic.

III. Should Applicants elect either Group VII or Group VIII, this application contains claims directed to the following patentably distinct species of administration:

A <u>single</u> specific species of administration that does not contain another species among the various species recited in claims 19-24.

The species are independent or distinct because they are distinct administration routes involving different starting materials or formulations that can influence the desired end-results.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, at least claims 14 and 50 are generic.

Additionally, this application contains claims directed to the following patentably distinct species of co-administered material:

A specific named co-administered material recited in the Markush group of claim 30 or 58.

The species are independent or distinct because they are distinct materials that are different chemically, physically and properties.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, at least claims 14, 30, 50 and 58 are generic.

Moreover, this application contains claims directed to the following patentably distinct species of groups modified at the 2' position:

A <u>single</u> specific named group that does not contain another species recited in claims 68-70.

The species are independent or distinct because they are structurally distinct one from the others.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, at least claims 61, 65 and 66 are generic.

IV. Should Applicants elect either Group IX or Group X, this application contains claims directed to the following patentably distinct species of promoters:

A specific named promoter recited in the Markush group of claim 27 or 55.

The species are independent or distinct because they are distinct promoters that have different sequences and properties.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, at least claims 25-29 and 53-57 are generic.

Additionally, this application contains claims directed to the following patentably distinct species of recombinant viral vector:

A specific named recombinant viral vector recited in the Markush group of claim 28 or 56.

The species are independent or distinct because they are distinct recombinant viral vectors that are different chemically, physically and properties.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, at least claims 25-28 and 53-56 are generic.

Should Applicants elect retroviral vector as the aforementioned species above, this application contains claims directed to the following patentably distinct species of recombinant retroviral vector:

A specific named recombinant retroviral vector recited in the Markush group of claim 29 or 57.

The species are independent or distinct because they are distinct recombinant retroviral vectors that are different chemically, physically and properties.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, at least claims 25-29 and 53-57 are generic.

V. Should Applicants elect either Group XI or Group XII, this application contains claims directed to the following patentably distinct species of cells being transfected:

(a) chronic lymphocytic leukemia cells; (b) prostate cancer cells; (c) hematopoietic stem cells.

The species are independent or distinct because they are distinct cells that have different properties.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, at least claims 40-47 are generic.

Additionally, this application contains claims directed to the following patentably distinct species of promoters:

A specific named promoter recited in the Markush group of claim 44.

The species are independent or distinct because they are distinct promoters that have different sequences and properties.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, at least claims 40-49 are generic.

Moreover, this application contains claims directed to the following patentably distinct species of recombinant viral vector:

A specific named recombinant viral vector recited in the Markush group of claim 46.

The species are independent or distinct because they are distinct recombinant viral vectors that are different chemically, physically and properties.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, at least claims 40-46 and 48-49 are generic.

Should Applicants elect retroviral vector as the aforementioned species above, this application contains claims directed to the following patentably distinct species of recombinant retroviral vector:

A specific named recombinant retroviral vector recited in the Markush group of claim 47.

The species are independent or distinct because they are distinct recombinant retroviral vectors that are different chemically, physically and properties.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, at least claims 40-49 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's primary, Celine Qian, Ph.D., may be reached at (571) 272-0777, or SPE, Dave Nguyen, at (571) 272-0731.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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QUANG NGUYEN PH.D
PATENT EXAMINER